

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 January 2003 (03.01.2003)

PCT

(10) International Publication Number
WO 2003/000735 A3

(51) International Patent Classification⁷: C12N 15/12,
5/10, C07K 14/705, 16/40, C12Q 1/68, G01N 33/50,
A61K 45/00, 39/00

(74) Agents: CARROLL, Alice, O. et al.; Hamilton, Brook,
Smith & Reynolds, P.C., 530 Virginia Road, P.O. Box 9133,
Concord, MA 01742-9133 (US).

(21) International Application Number:
PCT/TB2002/002481

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 24 June 2002 (24.06.2002)

(25) Filing Language: English

(26) Publication Language: English

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

(30) Priority Data:
60/301,095 26 June 2001 (26.06.2001) US
60/332,758 6 November 2001 (06.11.2001) US

(71) Applicant (*for all designated States except US*): DECODE
GENETICS EHF. [IS/IS]; Sturlugotu 8, 101 Reykjavik
(IS).

Published:

— with international search report

(72) Inventors; and

(88) Date of publication of the international search report:
22 July 2004

(75) Inventors/Applicants (*for US only*): MARTINEZ,
Roger, A., Moraga [ES/DE]; Bleichstrasse 6, 60313
Frankfurt am Main (DE). SIGURDSSON, Gunnar, Thor
[IS/IS]; Kjarrholmi 8, IS-200 Kopavogur (IS).

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*



WO 2003/000735 A3

(54) Title: NUCLEIC ACIDS ENCODING OLFACTORY RECEPTORS

(57) Abstract: Nucleic acids encoding G protein-coupled receptors are disclosed, and methods of using same.

INTERNATIONAL SEARCH REPORT

Intern..... Application No
PCT/IB 02/02481

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N5/10 C07K14/705 C07K16/40 C12Q1/68
G01N33/50 A61K45/00 A61K39/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, SEQUENCE SEARCH, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | WO 01 27158 A (FUCHS TANIA ;GLUSMAN GUSTAVO (IL); LANCET DORON (IL); YEDA RES & D) 19 April 2001 (2001-04-19) SEQ ID NO: 691 & 1623 --- | 1-52 |
| X | DATABASE EMBL20 June 2000 (2000-06-20) SYCAMORE N: "Human DNA sequence from clone RP11-542K23 on chromosome 9" Database accession no. AL359636 XP002231347 Positions 138690 - 139610 --- -/-- | 1-52 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

24 February 2003

Date of mailing of the international search report

15. 05. 2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bucka, A

INTERNATIONAL SEARCH REPORT

Inter.....al Application No
PCT/IB 02/02481

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>DATABASE EMBL10 March 1998 (1998-03-10) GIORGI D G; ROUQUIER S P: "Homo sapiens olfactory receptor (OR1-26) gene, partial cds." Database accession no. U86216 XP002231348 the whole document</p> | 1-52 |
| X | <p>-& ROUQUIER S ET AL.: "Distribution of olfactory receptor genes in the human genome" NATURE GENETICS, NEW YORK, NY, US, vol. 18, no. 3, March 1998 (1998-03), pages 243-250, XP002111208 ISSN: 1061-4036 the whole document</p> | 1-52 |
| P,X | <p>--- WO 01 68805 A (SENO MYX INC) 20 September 2001 (2001-09-20) * AOLFR250 sequences * page 189</p> | 1-52 |
| P,X | <p>--- WO 01 90359 A (INCYTE GENOMICS INC ;KALLICK DEBORAH A (US); PATTERSON CHANDRA (US) 29 November 2001 (2001-11-29) SEQ ID NO: 7 & 30</p> | 1-52 |
| P,X | <p>--- WO 02 06345 A (ALSOBROOK JOHN P II ;BURGESS CATHERINE E (US); MACDOUGALL JOHN R () 24 January 2002 (2002-01-24) SEQ ID NO: 13 & 14 page 26 -page 33</p> | 1-52 |
| X | <p>--- DATABASE EMBL25 April 2000 (2000-04-25) YASUOKA ET AL.: "Rattus norvegicus gust43 gene for gustatory receptor 43, complete cds." Database accession no. AB038167 XP002231349 the whole document</p> | 1-52 |
| A | <p>--- ABE K ET AL: "PRIMARY STRUCTURE AND CELL-TYPE SPECIFIC EXPRESSION OF A GUSTATORY G PROTEIN-COUPLED RECEPTOR RELATED TO OLFACTORY RECEPTORS" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 268, no. 16, 5 June 1993 (1993-06-05), pages 12033-12039, XP000857320 ISSN: 0021-9258 the whole document</p> <p>---</p> | 1-52 |

-/--

INTERNATIONAL SEARCH REPORT

Inter... Application No
PCT/IB 02/02481

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>DATABASE EMBL9 April 1996 (1996-04-09) THOMAS M B: "Rattus norvegicus taste bud receptor protein TB 334 (TB 334) gene, complete cds." Database accession no. U50947 XP002231350 the whole document</p> | 1-52 |
| X | <p>-& THOMAS M B ET AL.: "Chemoreceptors expressed in taste, olfactory and male reproductive tissues" GENE: AN INTERNATIONAL JOURNAL ON GENES AND GENOMES, ELSEVIER SCIENCE PUBLISHERS, BARKING, GB, vol. 178, no. 1, 31 October 1996 (1996-10-31), pages 1-5, XP004043330 ISSN: 0378-1119 the whole document</p> | 1-52 |
| X | <p>--- DATABASE EMBL21 October 1999 (1999-10-21) SHARON D ET AL.: "Gorilla gorilla isolate PPOR1P1 olfactory receptor gene, partial cds." Database accession no. AF101763 XP002231351 the whole document -& SHARON DROR ET AL.: "Primate evolution of an olfactory receptor cluster: Diversification by gene conversion and recent emergence of pseudogenes" GENOMICS, ACADEMIC PRESS, SAN DIEGO, US, vol. 61, no. 1, 1 October 1999 (1999-10-01), pages 24-36, XP002180154 ISSN: 0888-7543 the whole document</p> | 1-52 |
| A | <p>--- FUCHS TANIA ET AL: "The human olfactory subgenome: From sequence to structure and evolution" HUMAN GENETICS, BERLIN, DE, vol. 108, no. 1, January 2001 (2001-01), pages 1-13, XP002178958 the whole document</p> <p>---</p> <p>-/--</p> | 1-52 |

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 02/02481

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | <p>TRASK B J ET AL: "Members of the olfactory receptor gene family are contained in large blocks of DNA duplicated polymorphically near the ends of human chromosomes"</p> <p>HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 7, no. 1, January 1998 (1998-01), pages 13-26, XP002135641</p> <p>ISSN: 0964-6906</p> <p>the whole document</p> <p>-----</p> | 1-52 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/02481

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 31 and 37 to 39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-52 (all partially and insofar as applicable)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 18 to 24, 26, 29 to 31, 33, 34 and 37 to 39 relate to compounds ("an agent") defined by reference to a desirable characteristic or property, namely their property to alter the activity of the claimed protein or to influence its expression.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to antibodies and ribozymes, as referred to in claims 18 and 23, and antisense nucleic acids, as mentioned in claim 30.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-52,
all partially and insofar as applicable

an isolated olfactory G protein-coupled receptor having the amino acid sequence SEQ ID NO: 2, isolated nucleic acids encoding said protein, represented by SEQ ID NO:1, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

Inventions 2 to 115: claims 1-52,
all partially and insofar as applicable

an isolated olfactory G protein-coupled receptor, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it,
wherein each separate invention is represented by an odd numbered polynucleotide sequence comprising SEQ ID NO: 3 to 229 and an even numbered protein sequence comprising SEQ ID NO: 4 to 230,
wherein invention 2 is represented by SEQ ID NO: 3 and 4, invention 3 is represented by SEQ ID NO: 5 and 6, continuing to invention 115, represented by SEQ ID NO: 229 and 230

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/02481

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|---|---------------------|----------------------------|---------------------|
| WO 0127158 | A | 19-04-2001 | AU 1326201 A | 13-02-2001 |
| | | | AU 2903701 A | 23-04-2001 |
| | | | AU 6118100 A | 13-02-2001 |
| | | | WO 0107093 A1 | 01-02-2001 |
| | | | WO 0107094 A1 | 01-02-2001 |
| | | | WO 0127158 A2 | 19-04-2001 |
| ----- | | | | |
| WO 0168805 | A | 20-09-2001 | AU 4736601 A | 24-09-2001 |
| | | | CA 2401406 A1 | 20-09-2001 |
| | | | EP 1299528 A1 | 09-04-2003 |
| | | | WO 0168805 A2 | 20-09-2001 |
| ----- | | | | |
| WO 0190359 | A | 29-11-2001 | AU 6181401 A | 03-12-2001 |
| | | | AU 6472101 A | 26-11-2001 |
| | | | CA 2408134 A1 | 22-11-2001 |
| | | | CA 2408140 A1 | 29-11-2001 |
| | | | EP 1301595 A2 | 16-04-2003 |
| | | | EP 1297128 A2 | 02-04-2003 |
| | | | WO 0187937 A2 | 22-11-2001 |
| | | | WO 0190359 A2 | 29-11-2001 |
| ----- | | | | |
| WO 0206345 | A | 24-01-2002 | AU 7355801 A | 30-01-2002 |
| | | | WO 0206345 A2 | 24-01-2002 |
| ----- | | | | |